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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	21

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/708,352	LEONARD ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,24 and 27* is/are pending in the application.

4a) Of the above claim(s) *13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 21-22, 24 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2003 has been entered. Applicant's amendment and response is acknowledged. Claims 3, 5-6, 8, 10, 21 and 27 have been amended.

Rejection Withdrawn

2. In view of Applicant's response, the rejection of claims 4 and 6-7 under 35 U.S.C. 102(a), pages 2-4 of paper no.12, mailed January 23, 2003 is withdrawn.

New Grounds of Rejection

Claim Objections

3. Applicant is advised that should claim 8 be found allowable, claim 22 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

4. Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 does not further limit the structure of the product composition and are intended use only and do not limit the structure of the product.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-12, 21-22, 24 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The claims are drawn to a vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipient and wherein

the vaccine does not include saponin. The amended claims contain new matter. The specification has recited saponin as an adjuvant that may be included in the claimed vaccine composition. It should be noted that saponin can be used as an adjuvant or it can be used as a detergent. The concepts are different. Therefore, a composition that does not contain saponin is different from a composition that does not comprise saponin as an adjuvant. The "new genus" in which the vaccine per se, rather than adjuvant component as saponin is the excluded material is not supported by the original disclosure. Applicant is required to cancel the new matter in the reply to this Office Action.

Response regarding new matter is addressed below:

Applicant urges that the MPEP section 2173.05(i) states that " the current view of the courts is that there is nothing inherently ambiguous or uncertain about a negative limitation so long as the boundaries of the patent protection sought are set forth definitely, albeit negatively, the claim complies with the requirements of 35 U.S.C. 112, second paragraph. Applicant urges that "...any negative limitation or exclusionary proviso must have basis in the original disclosure.

Applicant's arguments filed May 21, 2003 have been fully considered but they are not persuasive. The applicant's arguments are not commensurate in scope with the disclosure or claims. The claimed invention is drawn to an vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least on inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipent and wherein the vaccine does not include saponin. It is true, that "alternative

elements are positively recited in the specification, they may be explicitly excluded in the claims". However, the specification teaches at page 8, lines 14-21, that saponin is an adjuvant included in a Markush group of adjuvants. The claims as amended comprise a vaccine composition that does not include saponin. The claims as amended include a new genus of vaccines which does not include saponin which is not supported by the instant specification. As stated above, saponin can be used as an adjuvant or it can be used as a detergent. Therefore, a conception of a composition that does not contain saponin is different from a composition that does not comprise saponin as an adjuvant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8-12, 21-22 and 24 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims. Claim 8 is indefinite because it is not clear as to whether there are one or two pharmaceutically acceptable excipients included in the vaccine composition since claim 8 is dependent from claim 1. Clarification is required.

7. Claims 1-12, 21-22, 24 and 27 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "biotypes". It is not clear as to what applicant is referring? Clarification is required.

The following art rejections are made because of the following reasons: The specification states that the term "biotypes" means that a variant of a species, i.e. strain can be distinguished by one or more characteristics (page 5). The claims and the specification have not clearly defined the characteristics that distinguish biotype A, biotype B and biotype C from each other.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 3, 5-6, 21, 24 and 27 are rejected under 35 U.S.C. 102(b) as anticipated by Boothby, *(Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982).*

Claims 1, 3, 5-6, 21, 24 and 27 are drawn to a vaccine composition which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at

least one inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipient and wherein the vaccine does not include saponin.

Boothby teaches a vaccine composition comprising killed *Mycoplasma bovis* and phosphate buffered saline (PBS) used for systemic immunization of calves (page 130). Boothby teaches that the vaccine preparations used contained 5.00 mg/ml of antigen for immunization (page 131) which meets the claim limitation " wherein the amount of each inactivated biotype is at least 10^8 *M. bovis* cells". Boothby teaches that cows vaccinated with *M. bovis* antigen in PBS elicited a moderate indirect hemagglutinations (IHA) response to systematic vaccination, an IgG ELISA response and an ELISA IgA response (page 133). Booth by et al teach that the highest respiratory IgA reactivity was found in the nasal secretions of the group which was vaccinated with *M. bovis* in PBS (page 134). Boothby et al teach that there was no sign of respiratory illness in any calves used in the study (page 136). Therefore, the vaccines were protective against respiratory infection caused by *M. bovis.*

Since the Office does not have the facilities for examining and comparing applicant's vaccine with vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the products of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 1, 4, 5 and 7 are rejected under 35 U.S.C. 102(b) as anticipated by Thorns et al *(Res. Vet. Sci., 1980, 29(3), 328-332).*

Claims 1, 4 and 7 are drawn to a vaccine composition which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipient and wherein the vaccine does not include saponin.

Thorns et al teach attenuated bovine strains of *M. bovis*. Thorns et al teach that mice were inoculated with 0.1 of E medium (excipient) containing a known number of colony forming units (CFU) of *M. bovis.* Thorns et al teach that the attenuated strains (passaged more than 91-138 times) contained an inoculum per gland of 6.0-7.0 cells (cells measured (log_{10})(see Table 1, page 329). This amount meets the claim limitation "wherein the amount of each attenuated biotype is at least 10^5 *M. bovis* cells. Thorns et al teach that the *M. bovis* strains were passaged in liquid medium more than 60 times were markedly less virulent than the same or different strains with fewer passages. Thorns et al teach that the high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals (see the Abstract). Thorns et al teach that mice inoculated with high passage *M. bovis* did not produce a systemic response (page 331). Thorns et al teach that only one out of five in each of the group inoculated with *M. bovis* passaged 91 times showed signs inflammation (page 329, Table 1). Thorns et al teach that all mice that were inoculated with M. bovis passaged over 91 times had normal glands and showed not signs of systematic response (page 329, Table 1). Therefore, the mice vaccinated with *M. bovis*

passaged over 91 times appeared to be protected against systematic response. Thorns et al teach that the modified strains of *M. bovis* (high passage strains) should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease (page 332).

Since the Office does not have the facilities for examining and comparing applicant's vaccine with vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the products of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejection - 35 USC 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-12, 21-22, 24 and 27 are rejected under 35 U.S.C. 103(a) as unpatentable over Boothby *(Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982)* in view of Poumarat et al *(Veterinary*

Microbiology, 40, 1994, 305-321) further in view of Thorns et al *(Res. Vet. Sci., 1980, 29(3), 328-332).*

Claims 1-12, 21-22, 24 and 27 are drawn to a vaccine composition which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipient wherein the vaccine does not include saponin and further comprising a suitable adjuvant.

Boothby teaches a vaccine composition comprising killed *Mycoplasma bovis* and phosphate buffered saline used for systemic immunization of calves (page 130). Boothby also teaches vaccine preparations comprising 0.5 ml killed *Mycoplasma bovis* antigen, 1 ml of Freund's incomplete adjuvant and 0.5ml of various aqueous solutions (page 131). Boothby teaches that the vaccine preparations used contained 5.00 mg/ml of antigen for immunization (page 131) which meets the claim limitations " wherein the amount of each inactivated biotype is at least 10^8 *M. bovis* cells". Boothby teaches that *M. bovis* is not highly immunogenic in the bovine. Boothby teaches that immunopotentiating effect of adjuvants may be used to prolonged deposition of antigen, modification the antigen or the recruitment and/or activation of the circulating lymphoid or reticuloendothelial cells (page 129). Boothby teach that adjuvants have been used in successful vaccine preparations of *M. bovis* and other pathogenic mycoplasmas. Boothby further teaches that adjuvants would be of particular benefit if found for local immunization where lymphocytes and phagocytic cells are suppressed or where small amounts of antigen is preferred to avoid undesirable reactions (page 129).

Boothby does not teach the use of at least inactivated *M. bovis* biotypes.

Poumarat et al disclose 37 *Mycoplasma bovis* strains from 13 different genomic groups (i.e. biotypes)(see the Abstract). Poumarat et al disclose that based on the combination of the different electrophoretic profiles obtained with the three enzymes, the 37 strains could be classified in 13 genomic groups (table 2).

Boothby and Poumarat et al do not teach the use of attenuated *M. bovis* biotypes.

Thorns et al teach attenuated bovine strains of *M. bovis*. Thorns et al teach that mice were inoculated with 0.1 of E medium containing a known number of colony forming units (CFU) of *M. bovis.* Thorns et al teach that the attenuated strains (passaged more than 60 times) contained an inoculum per gland of 5.1-7.0 cells (cells measured (log_{10})((see Table 1, page 329). This amount meets the claim limitation "wherein the amount of each attenuated biotype is at least 10^5 *M. bovis* cells. Thorns et al teach that the *M. bovis* strains were passaged in liquid medium more than 60 times were markedly less virulent than the same or different strains with fewer passages. Thorns et al teach that the high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals (see the Abstract). Thorns et al teach that the modified strains of *M. bovis* (high passage strains) should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease (page 332).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the attenuated *M. bovis* strains of a taught by

Thorns et al and the multiple *M. bovis* biotype isolates as taught by Poumarat et al and modify the vaccine composition comprising inactivated *M. bovis* and PBS to include a suitable adjuvant because Poumarat et al teach that there is a marked intraspecies genomic heterogeneity among isolates of *Mycoplasma bovis* collected from different geographic origins and that antigenic variability must be taken into account in developing diagnostic and vaccination strategies (page 319) and Thorns et al has demonstrated that high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals and do not cause systematic changes in inoculated animals. Additionally, Boothby teaches that immunopotentiating effect of adjuvants may be used to prolonged deposition of antigen, modification the antigen or the recruitment and/or activation of the circulating lymphoid or reticuloendothelial cells (page 129). It would be expected that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, attenuated *M. bovis* strains of multiple biotypes, PBS and a suitable adjuvant would be effect against infections caused by *M. bovis.*

Status of Claims

11. No claims allowed.

Conclusion

12. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
August 20, 2003

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